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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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08/932,227 09/17/97 FOSSEL

E

EXAMINER

IM22/0510

MULLIS, J

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BOSTON MA 02109

ART UNIT

PAPER NUMBER

1711

8

DATE MAILED: 05/10/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

08/932,227

Applicant(s)

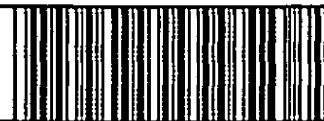
Fossel

Examiner

Jeffrey Mullis

Group Art Unit

1711



☒ Responsive to communication(s) filed on Feb 23, 1999

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire three month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 33-60 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 33-60 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Art Unit 1711

All remaining rejections and/or objections follow.

Claims 33-60 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

See the previous Office action at page 2, lines 6 et seq.

Claims 35-38, 44 and 53-55 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. See the previous Office action at the paragraph bridging pages 2 and 3.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject

Art Unit 1711

matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 33-34, 38, 39, 51-54, 56, 59 and 60 are rejected under 35 U.S.C. 102(a) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Weuffen et al. (USP 5,629,002).

See the previous Office action at page 4 line 5 et seq.

Claims 33-34 and 39 are rejected under 35 U.S.C. 102(a) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Hechtman (USP 5,595,753).

See the previous Office action at the paragraph bridging pages 4 and 5 et seq.

Claims 33-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Garfield et al. in view of Hechtman (USP 5,595,753), Altadonna (USP 5,853,768), Cook et al. (USP 5,428,070), Saavedra et al. (USP 5,632,981).

Garfield et al. disclose a process for healing wounds, treating impotence and restoring hair growth by topical application of an active ingredient. Note column 6 line 40 - column 5 line 50. The active ingredient is a nitric oxide donor at column 6 lines 4-22. Excipients such as salt solutions for influencing osmotic pressure and vegetable oils may be added and the composition may be in the form of transdermal patches at

Art Unit 1711

column 8 line 65 - column 9 line 5. Since the application of nitric oxide increases blood flow, increasing blood flow would be inherent in the reference.

Hechtman discloses that arginine may be applied topically to enhance nitric oxide production in tissues requiring such (Abstract, column 9 lines 56-61) and is taught to be particularly safe in comparison to other nitric oxide precursor substances (column 2 lines 9-18).

Cook et al. disclose that arginine glutamate functions to release nitric oxide in tissues requiring such (column 4 lines 17-30).

Altadonna (USP 5,853,768) discloses that iodide salts increase penetration of topically applied medicaments. Note the Abstract.

Saavedra et al. Disclose treating impotence by placing a nitric oxide generating substance inside a condom and then placing a condom on the penis at column 10, lines 20-35.

Garfield et al. do not disclose the use of arginine or the use of ionic salts to increase penetration or the use of arginine glutamate or application of nitric oxide realeasing substances to the penis.

It would have been obvious to a practitioner having an ordinary skill in the art at the time of the invention to use the

Art Unit 1711

arginine of Hechtman in the process of Garfield et al. motivated by Hechtman's disclosure that arginine functions to release nitric oxide as do the materials of Garfield et al. by the benefit of increased safety as disclosed by Hechtman and the expectation of extending the benefit of increased safety to the composition and process of Garfield et al. absent any showing of surprising or unexpected results.

It would have been obvious to a practitioner having an ordinary skill in the art at the time of the invention to use the arginine glutamate of Cook et al. in the process of Garfield et al. motivated by Cook et al.'s disclosure that arginine glutamate functions to release nitric oxide in tissue by the consequent expectation that arginine glutamate of Cook et al. would function as well as the nitric oxide releasing materials of Garfield et al. in the process of Garfield et al. absent any showing of surprising or unexpected results.

It would have been obvious to a practitioner having an ordinary skill in the art at the time of the invention to add salts to the composition of Garfield et al. as taught by Altadonna in order to obtain the benefit of increase penetration absent any showing of surprising or unexpected results.

It would have been obvious to a practitioner having an ordinary skill in the art at the time of the invention to apply the composition of Garfield et al. as modified by the secondary

Art Unit 1711

references to the penis as taught by Saavedra et al. motivated by the need to treat impotence as taught by Garfield et al. by Saavedra's disclosure that this could be done by topical application to the penis absent any showing of surprising or unexpected results.

Applicant's arguments filed 2-23-99 have been fully considered but they are not deemed to be persuasive.

The Examiner acknowledges the existence of applicant's copending applications. Applicant argues that claim 39 is neither in the alternative nor is it in combination. Applicant also argues that the words "or" and "combined" do not appear in the claim. However the Examiner does not understand how this is an argument that the claims are clear in that if these words do not appear in the claim, it is not clear if all the materials recited in these claims need be present or if only a single one of them need be present. With regard to claim 47, applicant makes a similar argument and states that "this claim is neither written in the alternative nor does the applicant wish to imply the combination of materials". However it is not clear to the Examiner what this claim does embrace if applicant is not reciting alternatives and is also not reciting a combination. There are only two alternatives, namely materials cited in the alternative and materials cited in combination.

Art Unit 1711

With regard to the question of whether applicant's concentrations of salt embrace 0 concentrations, applicant argues that 0 concentrations of salt would not work in a delivery mechanism that uses a high ionic strength to force the L-arginine out of the delivery vehicle into the tissue. However the above rejection has nothing to do with enablement and in any case it is not clear what delivery mechanism which uses high ionic strength has to do with the claims. Applicants argue that the claims of the instant invention teach the use of a high ionic strength environment. However no such limitation appears in the claims. Applicant argues that such an increase in efficiency is patentable. However such an argument relates to obviousness and not to clarity of the claims.

With regard to the issue of enablement, applicant argue that page 3 of the specification discloses that a salt may be used in the form of a cream. It is clear that use of a salt is enabled, however there is nothing in this passage that indicates combination with a hydrophobic delivery vehicle. Applicant argues that a base cream is disclosed in which some of the ingredients are hydrophobic. While it may be true that some of the materials are inherently hydrophobic, it is not clear that a cream which is hydrophobic is disclosed in that hydrophilic materials such as water are also disclosed. Furthermore the term "delivery vehicle" is broader than the term "cream" and

furthermore the disclosure of a single hydrophobic material cannot be said to enable the disclosure of hydrophobic delivery vehicles.

With regard to the rejection relying on Weuffen et al., applicants argue that there is nothing in the reference discussed in conjunction with promotion of hair growth. However column 14 lines 58-60 specifically discloses that the preparations were applied as a hair pack. Furthermore, column 14 lines 61-65 specifically refers to hair growth effect. While the effect is ascribed to thiocyanate, the composition specifically is taught to include arginine at column 14, lines 45-50 which is a nitric oxide releasing substance. With regard to applicant's argument regarding "an hostile biophysical environment", the instant claims do not require this and in any case such would appear to be inherent in the reference in that salts are present.

With regard to Hechtman, again applicants argue that a hostile biophysical environment is not disclosed by the reference. Again however the claims do not require such and with regard to applicant's argument that patentees' electrolyte solution would not necessarily have a high enough ionic strength to create such an environment, this is applicant's burden to prove.

The Examiner acknowledges that the inventor feels that all the references in the instant specification are not relevant. It

Serial No. 08/932,227

- 9 -

Art Unit 1711

is not necessary for applicant to submit these references given the fact that they are not relevant.

The Examiner acknowledges the existence of the PCT/US98/19429. The Examiner has reviewed the report submitted by applicant.

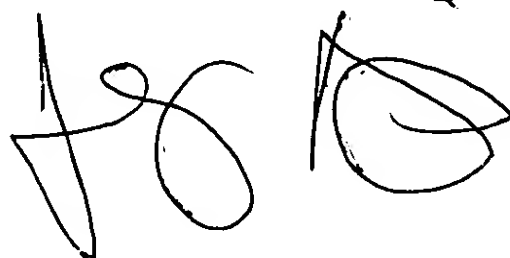
This Office action is not being made FINAL.

Any inquiry concerning this communication should be directed to Jeffrey Mullis at telephone number (703) 308-2820.

J. Mullis:cdc

May 4, 1999

JEFFREY C. MULLIS
PRIMARY EXAMINER
GROUP 1200-1711

A handwritten signature in black ink, appearing to be 'JCM', is written over the printed name and title of the examiner.